Amendment to the Claims

This listing of Claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently Amended) A method of crystallization, comprising the steps of:

a. introducing a first carrier-fluid into a first microchannel of a substrate;

b. introducing into a plug-forming region of the first microchannel:

1) a first ~~plug-~~fluid comprising a precipitant;

2) a second ~~plug-~~fluid comprising water; and

3) a third ~~plug-~~fluid comprising a crystallization target;

where each of the first, second and third ~~plug-~~fluids is substantially immiscible with the first carrier-fluid;

where pressure is applied when introducing each of the first, second and third ~~plug-~~fluids, and at least one of the first, second, and third ~~plug-~~fluids forms an interface with the first carrier fluid after the ~~plug-~~fluids contact the first carrier-fluid, where the interface has a capillary number sufficient to allow a plurality of plugs to form in the first microchannel in the first carrier-fluid, at least one of the plugs comprising the first, second and third ~~plug-~~fluids; and

where the crystallization target forms a crystal in the at least one of the plugs.

2. (Currently Amended) The method of claim 1, also comprising, before the crystallization target forms the crystal, the steps of:

a. introducing a second carrier-fluid into a second microchannel of the substrate;

b. introducing into a plug-forming region of the second microchannel:

1) a fourth ~~plug~~-fluid comprising a precipitant;

2) a fifth ~~plug~~-fluid comprising water; and

3) a sixth ~~plug~~-fluid comprising a crystallization target;

where each of the fourth, fifth and sixth ~~plug~~-fluids is substantially immiscible with second carrier-fluid;

where pressure is applied when introducing each of the fourth, fifth and sixth ~~plug~~-fluids, and at least one of the fourth, fifth and sixth ~~plug~~-fluids forms an interface with the second carrier fluid after the ~~plug~~-fluids contact the second carrier-fluid, where the interface has a capillary number sufficient to allow a plurality of plugs to form in the second microchannel in the second carrier-fluid, at least one of the plugs comprising the fourth, fifth and sixth ~~plug~~-fluids;

where the first and second microchannels merge into a common downstream microchannel;

where at least one plug flowing from the first microchannel merges with a plug flowing from the second microchannel upon entry into the downstream microchannel.

3. (Currently Amended) A method of crystallization, comprising the steps of:

a. introducing a first carrier-fluid into a first microchannel of a substrate;

b. introducing one or more first ~~plug~~-fluids into a first plug-forming region of the first microchannel to form a plug of a first plug type;

where the one or more first ~~plug~~-fluids comprise a precipitant and a crystallization target; and

where at least one plug of the first plug type comprises the precipitant and the crystallization target;

c. introducing one or more second ~~plug~~-fluids into either one of:

1) the first plug-forming region;

2) a second plug-forming region of the first microchannel; or

3) a second plug-forming region of a second microchannel;

where each of the ~~plug~~-fluids is substantially immiscible with the first carrier-fluid;

where the one or more second ~~plug~~-fluids form a plug of a second plug type at either one of the first plug-forming region, the second plug-forming region of the first microchannel, or the second plug-forming region of a second microchannel;

where the one or more second ~~plug~~-fluids comprise a precipitant;

where at least one of the plugs of the second plug type comprises ~~a~~ the precipitant;

where pressure is applied to the first and second microchannels when introducing the one or more first ~~plug~~ fluids and the one or more second ~~plug~~ fluids;

where at least one or more plugs of the first plug type alternate in sequence with one or more plugs of the second plug type; and

where the crystallization target forms a crystal in at least one of the at least one or more plugs of the first plug.

4. (Original) The method of claim 1 or 3, where the crystallization target is a member of the group consisting of protein, peptide, polynucleotide, oligonucleotide, subcellular organelle, subcellular protein complex, drug, small molecule/biological macromolecule complex, virus, colloidal particle, nanoparticle and combinations thereof.

5. (Original) The method of claim 1 or 3, where the crystallization target is a protein.

6. (Previously Presented) The method of claim 1 or 3, where each plug comprises a solvent, and there is solvent transfer from one plug into another plug.

7. (Currently Amended) The method of claim 6, where the solvent is water~~, and where the carrier fluid is permeable to water~~.

8. (Canceled)

9. (Currently Amended) The method of claim 3, where the one or more second ~~plug~~-fluids is introduced into at least one of the first plug-forming region and the ~~second plug-forming~~ second plug-forming region.

10. (Canceled)

11. (Currently Amended) The method of claim 3, where the one or more second ~~plug~~-fluids is introduced into the second microchannel of the second plug-forming region.

12. (Previously Presented) The method of claim 11, where the first and second microchannels merge into a common downstream microchannel, such that one or more plugs flowing from the first microchannel alternate with one or more plugs of the second plug type flowing from the second microchannel upon entry into the downstream microchannel.

13. (Currently Amended) The method of claim 9, where a second carrier-fluid is introduced into the first plug-forming region of the first microchannel so that it separates the one or more first ~~plug-~~fluids from the one or more second ~~plug-~~fluids prior to formation of any plug at the first plug-forming region.

14. (Currently Amended) The method of claim 13, where the second carrier-fluid is introduced through an inlet positioned between a first set of one or more inlets used for introducing one or more of the first ~~plug-~~fluids and a second set of one or more inlets used for introducing one or more of the second ~~plug-~~fluids.

15. (Currently Amended) The method of claim 1 or 3, where each of the carrier-fluids and ~~plug-~~fluids is introduced into the microchannels according to a respective flow rate under pressure, either directly into a microchannel or through an inlet feeding into a microchannel.

16. (Canceled)

17. (Original) The method of claim 15, where the pressure is halted after one or more plugs are formed.

18. (Canceled)

19. (Previously Presented) The method of claim 15, where at least one of the respective flow rates is varied relative to one another of the respective flow rates.

20. (Canceled)

21. (Currently Amended) The method of claim 15, where at least one of the ~~plug-~~fluids is introduced into a respective carrier-fluid at a variable respective flow rate.

22. (Currently Amended) The method of claim 15, where the respective flow rates are varied resulting in a plurality of plugs exhibiting a concentration gradient among the plurality of plugs with regard to one or more of the ~~plug-~~fluids.

23. (Previously Presented) The method of claim 1 or 3, where at least one of the microchannels has a turn.

24. (Currently Amended) The method of claim 3, where each of the carrier-fluids and ~~plug-~~fluids is introduced into the microchannels according to a respective flow rate under pressure, either directly into a microchannel or through an inlet feeding into a microchannel; and where one or more of the respective flow rates are varied so that the concentration of a first component in at least one of the plugs of one plug-type provides a correlative and quantitative measure of a second component in an adjacent plug.

25. (Canceled)

26. (Currently Amended) The method of claim 1 or 3, where at least one of the ~~plug-~~fluids comprises a salt.

27. (Previously Presented) The method of claim 3, where the salt concentration in the plug of the first plug type at the first plug-forming region is lower than the salt concentration in the plug of the second plug type at the plug-forming region where the plug of the second type is formed.

28. (Previously Presented) The method of claim 3, where the salt concentration in the plug of the first type at the first plug-forming region is at least 2 times lower than the salt concentration in the plug of the second plug type at the plug-forming region where the plug of the second type is formed.

29. (Previously Presented) The method of claim 3, where the salt concentration in the plug of the first type at the first plug-forming region is at least 5 times lower than the salt concentration in the plug of the second plug type at the plug-forming region where the plug of the second type is formed.

30. (Previously Presented) The method of claim 3, where the salt concentration in the plug of the first type at the first plug-forming region is at least 10 times lower than the salt concentration in the plug of the second plug type at the plug-forming region where the plug of the second type is formed.

31-33. (Canceled)

34. (Previously Presented) The method of claim 3, where a plug flowing pattern is obtained in which each of the plugs of the first plug type is adjacent to one plug of the second plug type.

35. (Canceled)

36. (Original) The method of claim 1 or 3, where at least one of the carrier-fluids comprises a fluorinated compound.

37-38. (Canceled)

39. (Original) The method of claim 38, where the component is selected from the group consisting of water, acid, base, buffer and solvent.

40. (Canceled)

41. (Canceled)

42. (Original) The method of claim 3, where the first and second carrier-fluids are the same.

43. (Previously Presented) The method of claim 3, where the first and second carrier-fluids are different.

44-50. (Canceled)

51. (Previously Presented) The method of claim 1 or 3, further comprising detecting the presence of the crystal in at least one of the plugs.

52. (Currently Amended) The method of claim 1 or 3, further comprising:

removing the crystal from the microchannel;

placing the crystal in a capillary tube; and

analyzing the crystal in ~~a~~ the capillary tube.

53-59. (Canceled)

60. (Currently Amended) The method of claim 1 or 3, where water ~~evaporates~~ is evaporated from the plugs.

61. (Original) The method of claim 1 or 3, where the substrate is soaked in water prior to crystal formation.

62. (Original) The method of claim 1 or 3, where the substrate is soaked in an aqueous salt solution prior to crystal formation.

63-74. (Canceled)

75. (Currently Amended) The method of claim 1 or 3, where each of the ~~plug~~ fluids comprises a solvent, and the solvent of each of the ~~plug~~ fluids is either the same or different.

76. (Currently Amended) The method of claim 1, where the plurality of plugs is formed in the first microchannel when the first ~~plug~~-fluid, the second ~~plug~~-fluid, and the third ~~plug~~-fluid are simultaneously introduced into the plug-forming region of the first microchannel.

77. (Currently Amended) The method of claim 1, where the first ~~plug~~-fluid, the second ~~plug~~-fluid, and the third ~~plug~~-fluid are introduced into the plug-forming region of the first microchannel to form a plurality of drops, the plurality of plugs is formed when at least two of the drops merge in the first microchannel.

78. (Previously Presented) The method of claim 1, where the capillary number is less than about 10.

79. (Previously Presented) The method of claim 78, where the capillary number is less than about 0.2.

80. (Currently Amended) A method of crystallization, comprising the steps of:

a. introducing a first carrier-fluid into a first microchannel of a substrate;

b. introducing into a first inlet in fluid communication with the first microchannel:

1) a first ~~plug~~-fluid comprising a precipitant; and

2) a second ~~plug~~-fluid comprising a crystallization target;

where each of the first and second ~~plug~~-fluids is substantially immiscible with the first carrier-fluid;

where pressure is applied when introducing each of the first and second ~~plug~~-fluids, and at least one of the first and second ~~plug~~-fluids forms an interface with the first carrier fluid after the ~~plug~~-fluids contact the first carrier-fluid, where the interface has a capillary number sufficient to allow a plurality of plugs to form in the first microchannel in the first carrier-fluid, at least one of the plugs comprising the first and second ~~plug~~-fluids; and

where the crystallization target forms a crystal in the at least one of the plugs.

81. (Currently Amended) The method of claim 80, where the first and second ~~plug~~-fluids form a laminar flow in the first inlet before the ~~plug~~-fluids contact the first carrier-fluid.

82. (Currently Amended) A method of conducting a reaction, comprising the steps of:

a. introducing a first carrier-fluid into a first microchannel of a substrate;

b. introducing into a first inlet in fluid communication with the first microchannel:

1) a first ~~plug~~-fluid comprising a first reagent; and

2) a second ~~plug~~-fluid comprising a second reagent;

where each of the first and second ~~plug~~-fluids is substantially immiscible with the first carrier-fluid;

where pressure is applied when introducing each of the first and second ~~plug~~-fluids, and at least one of the first and second ~~plug~~-fluids forms an interface with the first carrier fluid after the ~~plug~~-fluids contact the first carrier-fluid, where the interface has a capillary number sufficient to allow a plurality of plugs to form in the first

microchannel in the first carrier-fluid, at least one of the plugs comprising the first and second ~~plug~~-fluids; and

where the first and second reagent undergo a reaction in the at least one of the plugs.

83. (New) The method of claim 1, wherein the first fluid is separated from the third fluid by the second fluid when the fluids are introduced into the plug-forming region.

84. (New) The method of claim 1, wherein the fluids are simultaneously introduced into the plug-forming region via an inlet in fluid communication with the first microchannel.